

### STATUTORY DECLARATION

I, Sandra Therese Antoinette Kite-Malkowska, of 21 Broadway, Wilburton, Ely, Cambridge, CB6 3RT, Great Britain, do hereby solemnly and sincerely declare as follows:-

1. My curriculum vitae is given in Attachment 1.

I hold the position of Assistant Director, Formulation Laboratories in Napp Research Centre Limited, Cambridge, England, which position I have held since 1986.

2. The following experiments were carried under my supervision in order to prepare controlled release formulations according to the teaching of European Patent Application Publication No. 147780 and containing tramadol hydrochloride.

Tablets were prepared using the formula and process of Example 1 of EP 147780 but replacing the active ingredient L-dopa with tramadol hydrochloride, Example 1 was used as it was considered this formulation would be more appropriate for tramadol hydrochloride which would normally be dosed in the range of 100 to 400mg per unit dose. The formula and procedure were, in more detail:

#### Core Tablet

	mg/tablet
Tramadol hydrochloride	200
Microcrystalline cellulose Ph. Eur. (Avicel PH101)	150
Magnesium stearate Ph. Eur.	2.0
	<u>352</u>

The microcrystalline cellulose and tramadol hydrochloride were added to the glass jar of a tubula blender and blended for 10 minutes. The magnesium stearate was added to the jar and blended for 2 minutes.

Tablets were compressed using 3/8" round, shallow concave, bevelled edge tooling on a Killian rotary tablet machine to an average tablet weight of 352mg and 6kp hardness.

## Experiment 1

### Film Coat Formulation

	% w/w
Polyvinyl alcohol (superhydrolysed)*	2.00
Purified water Ph. Eur.	98

\* Airvol 165 (super hydrolysed) supplied by Air Products.

### Method of Preparation

The polyvinyl alcohol was dispersed in the cold, purified water and the dispersion was heated with stirring to boiling point. After the polyvinyl alcohol had fully dissolved the dispersion was cooled to room temperature.

### Coating conditions

Film coating was carried out using a Strea 1 Aerocoater using the following conditions:-

Inlet air temperature	75°C
Outlet air temperature	60°C
Atomising air pressure	2 bar
Fluid flow rate	3g/min
Coating time	50-55 min
Weight increase	5% w/w approximately

Atomising air pressure	2 bar
Fluid flow rate	3g/min
Coating time	50-55 min
Weight increase	5% w/w approximately

## EXPERIMENT 2

Tablets were prepared according to the procedure of Experiment 1 but using Polyvinyl alcohol ('fully hydrolysed') supplied by Honeywill and Stein.

### Dissolution Method

Ph. Eur. paddle method at 100 rpm using 0.1 N hydrochloric acid and detection by UV absorbance at 270nm.

The results obtained were as follows:-

	Product of Experiment No. 2	Product of Experiment No. 1
Hour		
1	88	59
2	98	91
3	99	102
4	99	107
5	99	109
6	99	110

AND I MAKE this solemn declaration conscientiously believing the same to be true and by virtue of the Oaths and Declaration Act 1957.

*Pandra Kite-Maukontha*  
DECLARED AT Merlin Place Centerville this date of 26/7/1995

Before me

*[Signature]* WMR

Solicitor authorised to take Statutory Declarations

RM/12/2650